



# Center for Regulatory Effectiveness

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November 24 , 2004

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Report on Carcinogens Program  
National Institute of Environmental Health Sciences  
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Dear Dr. Jameson:

Re: Comments on the atrazine nomination and revised RoC  
procedures for the 12<sup>th</sup> RoC in response to 69 FR 62276-79,  
Oct. 25, 2004

The Center for Regulatory Effectiveness ("CRE") submits the following additional comments on the above-referenced matters.

These CRE comments supplement those previously submitted by CRE on both the atrazine nomination and the procedures for the 12<sup>th</sup> Report on Carcinogens ("RoC"). These CRE comments also supplement, but do not supplant, the Data Quality Act ("DQA") Requests for Correction ("RFC") that CRE and other affected persons filed with NTP regarding the atrazine nomination and RoC procedures.<sup>1</sup> These CRE comments are in addition to the comments CRE is filing separately on the Talc nomination and RoC procedures in response to the above-referenced *Federal Register*

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<sup>1</sup> CRE's RFC regarding RoC procedures is available online at <http://aspe.hhs.gov/infoquality/request&response/16a.shtml>.  
CRE's RFC regarding atrazine is available online at <http://aspe.hhs.gov/infoquality/request&response/18a.shtml>  
NIH's responses so far to these RFCs are available online at <http://aspe.hhs.gov/infoquality/requests.shtml>

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notice. CRE will first comment on the atrazine nomination and second on NTP procedures.

### **ATRAZINE SHOULD BE WITHDRAWN FROM RoC REVIEW**

As demonstrated in CRE's RFCs and prior comments, NTP should announce that it is withdrawing atrazine for review in the 12<sup>th</sup> RoC.

The United States Environmental Protection Agency ("EPA") agrees with CRE. In comments filed during the initial comment period on the atrazine nomination, EPA recommended "that atrazine be removed from the list of additional agents for possible listing in the next edition of the RoC."<sup>2</sup>

Removal of atrazine from RoC review is necessary for the following reasons.

NTP stated publicly that it accepted atrazine for review in the 12<sup>th</sup> RoC for only one reason: "IARC finding of sufficient evidence of carcinogenicity in animals."<sup>3</sup> NTP's stated basis for accepting atrazine for review would not satisfy the RoC cancer classification criteria even if it were accurate.<sup>4</sup> The animal tests referenced in the IARC findings involved only one type of tumor at one site in one sex and in a single highly vulnerable rat species. The animal tests do not show or rely on multiple routes of exposure or an unusual degree with regard to incidence, site or type of tumor, or

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<sup>2</sup> EPA's comments are available online at <http://ntp.niehs.nih.gov/ntp/NewHomeRoc/RoC12/hazen-07-19-04.pdf>.

<sup>3</sup> NTP's stated basis for accepting atrazine for review in the 12<sup>th</sup> RoC is available online at <http://ntp-server.niehs.nih.gov/index.cfm?objectid=03C9B9E5-E172-1851-FE7CC3CA29D7F662>

<sup>4</sup> The RoC criteria are available online at <http://ntp-server.niehs.nih.gov/index.cfm?objectid=03C9CE38-E5CD-EE56-D21B94351DBC8FC3>

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age of onset.<sup>5</sup> Consequently, even as characterized by NTP, the IARC animal tests could not support atrazine RoC review, and NTP should withdraw atrazine from RoC review.<sup>6</sup>

Atrazine should also be withdrawn from review because NTP inaccurately and incompletely characterized IARC's findings. NTP omitted IARC's conclusion that "there is strong evidence" the mechanism by which atrazine causes one type of tumor in one type of rat is irrelevant to humans.<sup>7</sup> After years of review, EPA agreed that the rat tests were irrelevant to human cancer because they are caused by a mechanism of action that is not present in humans.<sup>8</sup> NTP's inaccurate and incomplete statement of IARC's findings, which is NTP's only basis for atrazine RoC review, does not comply with the requirements of the DQA; does not comply with OMB's government-wide DQA guidelines; does not comply with HHS's DQA guidelines; and does not comply with the National Institute of Health's DQA guidelines.<sup>9</sup> NTP's violation of the DQA and DQA guidelines requires that NTP retract its notice of RoC atrazine review. NTP cannot review atrazine in the RoC until and unless NTP states a basis for atrazine review that is supported by sound science and that meets DQA and DQA guidelines standards. There is no such basis now.

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IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, "Some Chemicals that Cause Tumors of the Kidney or Urinary Bladder in Rodents and Some Other Substances," Vol. 73, pp. 97-98 (1999)("IARC Monograph"), copy included in Appendix "A" to CRE's RFC on atrazine.

<sup>6</sup> See RoC criteria for classifying human carcinogens solely on the basis of animal tests at <http://ntp-server.niehs.nih.gov/index.cfm?objectid=03C9CE38-E5CD-EE56-D21B94351DBC8FC3>

<sup>7</sup> See footnote 5, *supra*, IARC Monograph at p. 99.

<sup>8</sup> Appendix B to CRE's RFC on atrazine, at p. 2; see Appendix "C" to CRE's RFC on atrazine at p. 13 (SAP Report to EPA on atrazine FIFRA review, chaired by Dr. Christopher Portier).

<sup>9</sup> The DQA is codified at 44 U.S.C. § 3516 historical and statutory notes. OMB's government-wide DQA guidelines are available online at [http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=2002\\_register&docid=R2-59-filed.pdf](http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=2002_register&docid=R2-59-filed.pdf) HHS's DQA guidelines are available online at <http://www.hhs.gov/infoquality/part1.html>. NIH's DQA guidelines are available online at [http://www.thecre.com/pdf/20020501\\_dhhs-nih.guidelines.pdf](http://www.thecre.com/pdf/20020501_dhhs-nih.guidelines.pdf)

After years of review, EPA recently concluded that atrazine is “not likely to be carcinogenic to humans.”<sup>10</sup> Researchers for the EPA, National Cancer Institute, and National Institute of Environmental Health and Safety recently “found no associations between cancer incidence and atrazine exposure, whether atrazine was analyzed as a cumulative measure (lifetime days of exposure) or as an intensity-weighted cumulative measure (intensity-weighted lifetime days of exposure).”<sup>11</sup> This conclusion is based on a massive epidemiological study of commercial and private atrazine applicators.<sup>12</sup> The overwhelming weight of scientific evidence is that atrazine is neither a known nor a reasonably anticipated human carcinogen, and these are the only two RoC cancer classifications.<sup>13</sup> Consequently, there is no basis or reason for reviewing atrazine in the 12<sup>th</sup> RoC, and the atrazine nomination should be withdrawn.

Finally, an essential step in RoC review is preparation and publication of a Background Document for the substance under review. For the reasons stated above, sound science and the DQA prevent NTP from preparing and publishing a Background Document that even suggests atrazine is a known or reasonably anticipated human carcinogen. Proceeding further on atrazine RoC review would, therefore, be a waste of agency and stakeholder time, effort, and resources. The atrazine nomination should be withdrawn from RoC review.

## 12<sup>TH</sup> RoC PROCEDURES

### A. RG1 Can Recommend and the Director Can Approve Termination of RoC Review at the Background Document Stage

CRE understands from the revised 12<sup>th</sup> RoC procedures posted on the NTP website that if RG1 determines the Background Document does not support classification of a substance under either of the two RoC cancer classifications, then RG1 will recommend to the Director that RoC review of the substance stop. RoC review of the substance will stop at this point if the Director approves RG1's recommendation. CRE requests that NTP inform us if this understanding of the<sup>12</sup> RoC procedures is incorrect.

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<sup>10</sup> See Appendix "B" to CRE's RFC on atrazine at p. 2.

<sup>11</sup> Rusiecki, J., *et al.*, *Cancer Incidence Among Pesticide Applicators Exposed to Atrazine in the Agricultural Health Study*, Journal of the National Cancer Institute, Vol. 96, No. 18, September 15, 2004, at p. 1380.

<sup>12</sup> *Id.* at p. 1376.

<sup>13</sup> Footnote 4, *supra*.

**B. DQA Pre-Dissemination Review Procedures Apply to the NTP's Statement of the Basis for Reviewing a Substance in the RoC and to RoC Background Documents; and Public Comment Should be Allowed on Draft Background Documents**

NTP's 12<sup>th</sup> RoC procedures must include predissemination review measures designed to ensure compliance with the requirements of the DQA and with the relevant agency DQA guidelines. Those predissemination review requirements apply to NTP's statement of why it is reviewing a substance for the RoC, and to the Background Document.

OMB's government-wide DQA Guidelines require that NTP establish a predissemination review process for the RoC:

"As a matter of good and effective agency information resources management, agencies shall develop a process for reviewing the quality (including the objectivity, utility, and integrity) of information before it is disseminated. Agencies shall treat information quality as integral to every step of an agency's development of information, including creation, collection, maintenance, and dissemination. This process shall enable the agency to substantiate the quality of the information it has disseminated through documentation or other means appropriate to the information."<sup>14</sup>

NIH's own DQA guidelines explain:

The OMB guidelines apply to official information (with the NIH imprimatur) that is released on or after October 1, 2002. They apply to information in all media — printed, electronic, audiovisual, verbal, and other. The Guidelines focus primarily on the dissemination of substantive information (i.e., reports, studies, summaries) rather than information pertaining to basic agency operations. Information that is disseminated at the request of NIH or with specific NIH approval through a contract or a grant is subject to these Guidelines. ***The Guidelines apply to preliminary information, and are not limited to information used in agency rulemaking.*** Examples are provided below of the kinds of information that the NIH considers to be covered and not covered by the OMB Information Quality Guidelines.<sup>15</sup>

The RoC is provided in the NIH DQA guidelines as one example of information covered by the DQA guidelines.<sup>16</sup>

NTP's notices that it has accepted a substance for RoC review, and RoC Background

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<sup>14</sup> 67 FR 8459 (Feb. 22, 2002).

<sup>15</sup> NIH DQA Guidelines, II, *supra* footnote 9 (emphasis added).

<sup>16</sup> NIH DQA Guidelines, II, *supra* footnote 9, V. 2. iv.

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Documents, are at least “preliminary information” subject to the DQA and guidelines. In fact, they are much more.

NTP’s *Federal Register* and other notices that it has accepted a substance for RoC review is a final agency action that triggers formal RoC proceedings at least through RG1 review of the Background Document. Those notices disseminate information about the reasons for review (e.g., IARC findings) that are subject to pre-dissemination review to ensure compliance with DQA and guideline requirements. CRE understands that NTP is reconsidering its notice accepting atrazine for RoC review. The only way to meet the DQA and DQA guidelines requirements is withdraw atrazine from review.

Any RoC Background Document is also much more than “preliminary information.” It is “the final document of record” for a substance that provides much of the basis for the review groups’ recommendations for RoC listing. NTP’s procedures for the 12<sup>th</sup> RoC state that

If the RG1 determines that the background document is adequate for use in reviewing the nomination and applying the criteria for listing in the RoC, ***it is then considered the final document of record and placed on the NTP RoC web site (<http://ntp-server.niehs.nih.gov>, select Report on Carcinogens)***. The NTP publishes a notice through the NTP list-serv and the NTP web site announcing the availability of the background document for a nomination. The review of a nomination by any of the formal review groups will not begin for at least 30 days after the announcement of the availability of the background document for that nomination. Comment received on a background document becomes part of the public record and, upon receipt, is added to the review package that is distributed to the formal review committees.<sup>17</sup>

Under the current RoC procedures, there will be no opportunity for public comment on a Background Document before it becomes “the final document of record” and RG1 uses it to make a recommendation on further RoC review. These procedures should be changed. Public comment on a draft Background Document should be allowed before it becomes final and before RG1 reviews it. NTP should respond in writing to all written comments and modify the draft Background Document, as warranted, based on public comments before the Document is used for any purpose. This process change would help NTP comply with the DQA and DQA guidelines pre-dissemination review requirements. It would also lead to more informed and more accurate decision making.

Finally, the administrative record for RoC review of any substance should clearly document the DQA pre-dissemination review that has been performed for each information

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<sup>17</sup> The NTP procedures for the 12<sup>th</sup> RoC are available online at <http://ntp-server.niehs.nih.gov/ntpweb/index.cfm?objectid=720162B0-BDB7-CEBA-FE2B27BB-A2785BA5> (emphasis added).

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dissemination relation to review of that substance. The United States Administrative Procedure Act requires that federal agency action be "in accordance with law." 5 U.S.C. § 706(2)(A). The DQA is a law with which NTP must comply when disseminating information. 44 U.S.C. § 3516 Historical and Statutory Notes. Compliance with that law must be demonstrated in the administrative record for the agency information dissemination. *See generally* Citizens to Preserve Overton Park, Inc. v. Volpe, 401 U.S. 402, 414, 416-20 (1971).

### CONCLUSIONS

NTP should withdraw atrazine from review in the 12<sup>th</sup> RoC.

NTP should allow public comment on draft Background Documents before RGI uses reviews them to recommend whether further RoC review should occur and before they become final documents of record. NTP should produce written responses to public comment on draft Background Documents. Draft Background Documents should be revised, as warranted, based on public comments before the Documents are used for any purpose.

The DQA and DQA guidelines predissemination review requirements apply to NTP's notice of the basis for accepting a substance for RoC review, and to RoC Background Documents.

NTP should document in the administrative record of each RoC information dissemination the measures NTP took to ensure compliance with the DQA and DQA guidelines predissemination review requirements.

Sincerely,



Scott Slaughter

Center for Regulatory Effectiveness